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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/872,165	06/01/2001	Peter C. Brooks	89188.0011	8769

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/872,165	BROOKS ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *6-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 36-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Re: Brooks *et al*
Priority Date: 01 June 2001

1. The amendment filed 9/10/2004 is acknowledged and entered into the record. Accordingly, claims 36-45 are newly added.

2. Claims 1-45 are pending, claims 6-35 are withdrawn as being drawn to a non-elected invention. Applicant is reminded to cancel all claims drawn to non-elected inventions.

3. Claims 1-5, and 36-45 are examined on the merits.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Maintained - 35 USC § 102

5. The rejection of claims 1-5 under 35 USC § 102(b) as being anticipated by Goldberg GI (WO 98/12309) is maintained for the reasons of record. It is noted that because claims 37-41 and 43-45 are newly rejected under 35 USC 112, 2nd paragraph as being vague and indefinite for having a narrow limitation followed by a broad limitation (see paragraph 8, below), that if applicant amends claims to read on "comprising" language, the instant rejection could be applied to claims 37-41, and 43-45.

Applicant argues that the amendment to the claims to recite "short anti-angiogeneic peptides" overcomes the anticipatory disclosure of Goldberg GI. Applicant argues that a short peptide "could have a size of 20 amino acids or fewer in length", and

points to the embodiments of the specification as support for this definition. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. Because the specification has not specifically limited the term "short" to be of any specific length and only provides examples by way of SEQ ID No: 1 and 2, and because the term "comprising" is used in the body of the claim, the peptide is broadly interpreted as a protein larger than 9-11 amino acids, such as the one taught by Goldberg GI. Furthermore, because the Goldberg GI teaches a protein that comprises SEQ ID No: 1 and because the claims have been amended to recite "biologically equivalent" sequences, in the absence of evidence to the contrary, the protein of SEQ ID No: 2 would also have the same biological activity.

Applicant also argues unexpected results (see page 14 of response) by stating "It is a discovery of the present invention that SEQ ID No: 1 and 2 unexpectedly inhibit angiogenesis and tumor growth." Applicant also states that the examiner acknowledged that the peptide is "*not involved in inhibiting angiogenesis*, metastasis, or a disease". Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. First, evidence of secondary considerations, such as unexpected results or commercial success, is irrelevant to 35 U.S.C. 102 rejections and thus cannot overcome a rejection so based. In re Wiggins, 488 F.2d 538, 543, 179 USPQ 421, 425 (CCPA 1973). Second, it is noted that the examiner stated in the office action mailed 5/6/2004, that Goldberg GI "does not specifically teach that the peptide sequences are involved in inhibiting angiogenesis, metastasis, or a disease", this is not to say that the peptides are "not involved in inhibiting angiogenesis, metastasis, or a

disease", as stated by the applicant. Goldberg GI teaches a peptide that comprises the sequence of SEQ ID No: 1 and teaches a peptide, in the absence of evidence to the contrary, that has the same biological activity as that of SEQ ID No: 1 or 2. Because the office does not have the facilities to prove other wise, and because the property of being anti-angiogeneic is an inherent property of the peptide, Goldberg GI anticipates the claims.

Claim Rejections Maintained - 35 USC § 102

6. The rejection of claims 1-5 under 35 USC § 102(b) as being anticipated by Brooks *et al* (WO 97/45137) is maintained for the reasons of record. It is noted that because claims 37-41 and 43-45 are newly rejected under 35 USC 112, 2nd paragraph as being vague and indefinite for having a narrow limitation followed by a broad limitation (see paragraph 8, below), that if applicant amends claims to read on "comprising" language, the instant rejection could be applied to claims 37-41, and 43-45.

Applicant argues that Brooks *et al* does not anticipate the instant invention because Brooks *et al* teaches a 222 amino acid sequence that "comprises the nine amino acids of SEQ ID No: 1 and the nine internal amino acids of SEQ ID No: 2" (see page 14 of response). Applicant again argues that the reference does not teach a "short peptide" and further states that larger peptide would not be expected to have the same biological activity as that instantly claimed peptide. Applicant continues by stating Brooks *et al* does not teach a peptide that has anti-angiogeneic activity. Applicant's

arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. Applicant's arguments are substantially similar to those already presented and rebutted above (see paragraph 5). The claims as currently interpreted do not limit the size of the peptide because of the term "comprising". Moreover, the specification nor the claims distinctly define what a "short" peptide would encompass. Furthermore, the independent claim does not limit the peptide to only peptides comprising SEQ ID No: 1 or 2, but are instead drawn to peptides that are "biologically equivalent" to SEQ ID No: 1 or 2, thus one of ordinary skill in the art would interpret this as any peptide, regardless of size. And finally, because it appears that SEQ ID No: 1 and the core internal core of SEQ ID No: 2 are derived from the protein taught by Brooks *et al* it would, in the absence of evidence to the contrary, have the same biological activity. Thus the rejection of claims under 35 USC 102(b) as being anticipated by Brooks *et al* is maintained for the reasons of record.

If applicant amends claims 37-41 and 43-45 to recite a peptide "comprising" the sequence of SEQ ID No: 1 or 2, the instant rejection would be applied to those claims because as stated in the response filed 9/10/2004, potentially several amino acids flank the C- and N-terminal ends of the sequences. However, the specification, nor the claims specifically preclude more that 23 amino acids as taught by Brooks *et al* (see page 64 and SEQ ID No: 17). Thus these claims would also be anticipated.

NEW ARGUMENTS

Claim Rejections - 35 USC § 112, 2nd paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 37-41 and 43-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 37-41 and 43-45 recites the broad recitation of comprising additional flanking amino acids, and the claims also recites a peptide consisting of SEQ ID No: 1 or 2 which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 112, 1st paragraph

10. Claims 1-5, 37-41, and 43-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide comprising SEQ ID No: 1 or 2, does not reasonably provide enablement for an anti-angiogeneic peptide comprising a sequence that is biologically equivalent to SEQ ID No: 1 or 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a peptide that is biologically equivalent to a sequence of SEQ ID No: 1 or 2. The claims are further limited to peptides that comprise an additional flanking amino acid, either at the N-terminal end, C-terminal end, or both ends. The specification teaches that SEQ ID No: 1 and parts of SEQ ID No: 2 are derived from MMP-2 (see page 9, lines 4-6).

However, the specification provides insufficient guidance and objective evidence to predictably enable one of skill in the art to make or use the invention as claimed.

First, the claims can be broadly interpreted as being drawn to any peptide so long as it has biologically equivalent activity. The claims, in part (i.e. claims 1-5), do not limit the peptide to a sequence that comprises the sequence of SEQ ID No: 1 or 2 or an sequence that comprises the core of SEQ ID No: 1. Moreover, the claims have been amended to reflect any sequence so long as the peptide has a "biologically equivalent" activity, and thus would include a whole world of peptides, such as endostatin or angiostatin, because such peptides also exhibit properties that are similar to those of SEQ ID No: 1 or 2, namely anti-angiogeneic activity. Those of skill in the art recognize that peptide chemistry and the use of peptides is a relatively unpredictable field. Furthermore, because the intended purpose of the claimed invention is for the treatment of cancer in vivo, one of skill would also recognize that the specification has not provided sufficient guidance in terms of how biologically equivalent peptides would function as intended.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to any peptide sequence with biologically equivalent function to SEQ ID No: 1 or 2, and applicant has not enabled all of these types of peptides because the applicant has not taught what these peptides are, how they function, and or how to make such peptides, nor has it been shown that all peptides claimed are capable of functioning as that which is being disclosed. Furthermore, because the claims do not limit the amino acids that flank the sequences, one of skill in the art cannot predictably determine if such peptides would have the same biological activity that is disclosed.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach which amino acid could be tolerated without affecting the "biological activity" of the peptide as claimed. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to use any and all peptides which are either "biologically equivalent" or the addition of flanking amino acids to SEQ ID No: 1 or 2. Therefore, in view of the lack of predictability of the prior art, the breadth of the claims and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in a paper filed 9/10/2004.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

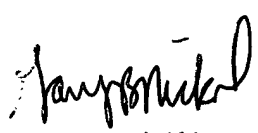
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art unit 1642
November 23, 2004



GARY NICKOL
PRIMARY EXAMINER